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EDITORIAL COMMENT

Radiofrequency Ablation of "Benign" Right Ventricular Outflow Tract Extrasystoles*

A Therapy That Has Found its Disease?

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Ventricular arrhythmias occur in the normal heart (1). For unclear reasons, the most frequently idiopathic ventricular arrhythmias originate from the right ventricular outflow tract (RVOT) (2). In some cases, the RVOT arrhythmias are manifested as multiple extrasystoles, couplets, and even short bouts of ventricular tachycardia (3) that usually are well tolerated and associated with mild extrasystolic palpitations or even no symptoms at all in as many as one-third of the patients (2). Nevertheless, these arrhythmias occasionally can be very symptomatic and invalidating. However, their long-term prognosis generally is considered as benign (4) despite exceptional reports of sudden death and ventricular fibrillation in adults and children (5–7).

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Before radiofrequency ablation (RFA), general agreement existed that no therapy was necessary for most patients with various forms of RVOT arrhythmias and that medical treatment was reserved only for very disabled patients. After RFA was shown highly effective in curing sustained and nonsustained forms of RVOT tachycardias (8), several investigators (9,10) applied this technique for treating high-grade RVOT ectopy. Zhu et al. (10) reported the first series of successful RFA of frequent, medically refractory, and severely symptomatic RVOT extrasystoles. The title of Wellens' editorial (11) ("Radiofrequency Catheter Ablation of Benign Ventricular Ectopic Beats: A Therapy in Search of a Disease") accompanying the Zhu et al. study (10) needs no further explanation and reflects the concern at the time regarding aggressive therapy for an arrhythmia with an excellent prognosis, usually responsive to conventional measures (4,11,12).

Are idiopathic RVOT arrhythmias actually so benign? Besides the exceptional occurrence of sudden death, recent case reports have questioned the effects of high-grade RVOT arrhythmias on left ventricular (LV) function. These reports described the occurrence of cardiomyopathy associated with RVOT ectopic activity (13–18). Idiopathic dilated cardiomyopathy rarely is associated with extrasystoles having a pattern of left bundle branch block with normal or inferior axis (19), suggesting that RVOT extrasystoles are unlikely a consequence of cardiomyopathy. More importantly, in all these reports, a dramatic improvement of LV function occurred after RFA of ventricular ectopy, suggesting that the cardiomyopathy actually resulted from the ventricular arrhythmia (13–18). The fact that patients without clinically apparent heart disease who have frequent ventricular ectopy frequently demonstrate subtle hemodynamic and/or angiographic abnormalities was first shown by Kennedy et al. (20) more than 20 years ago; however, the site of origin of the ventricular arrhythmia in these patients was not indicated. In a study originating from Wellens' laboratory, Lemery et al. (21) found hemodynamic signs of cardiac dysfunction in 45% of 47 patients with ventricular arrhythmias and no clinical evidence of heart disease. The investigators suggested that these abnormalities could be the result rather than the cause of the arrhythmias. Finally, Duffee et al. (22) were the first to report that suppression of frequent ventricular extrasystoles with antiarrhythmic drug therapy was associated with improvement of LV function in patients with presumed dilated cardiomyopathy.

The retrospective study reported by Takemoto et al. (23) in this issue of the *Journal* brings further support to the hypothesis that high-grade RVOT arrhythmias can cause LV dysfunction. During a 10-year period Takemoto et al. (23) studied a large population of 40 consecutive patients with monomorphic RVOT arrhythmias up to nonsustained ventricular tachycardia (<5 beats). The patients underwent a comprehensive investigation, including 24-h Holter monitoring, Doppler echocardiographic studies, exercise testing, coronary angiography, and/or thallium scintigraphy. The work-ups yielded normal results, suggesting the lack of clinically overt structural heart disease. Radiofrequency ablation was performed with standard techniques using pace-mapping (≥11 of 12 electrocardiography correlation) and strict success criteria. It was associated with a high acute success rate (93%) and a very low recurrence rate (3%). Holter and echocardiographic studies were then repeated 6 to 12 months after RFA.

The first important result in the study of Takemoto et al. (23) is the significant correlation between the LV end-diastolic dimension and the frequency of ventricular extrasystoles on a 24-h Holter before RFA. Such an association suggests that LV dysfunction was actually the result rather than the cause of the ventricular arrhythmia. Then, the investigators arbitrarily divided their data into three groups according to the tertiles of ventricular extrasystoles per 24 h ("lower group," <10% extrasystoles; "middle group," 10% to 20% extrasystoles; and "upper group" ≥20% extrasystoles). Patient selection might have been biased because the "upper group" represented approximately one-third of the study

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patients, an incidence that seems disproportionate to what is commonly observed in clinical practice.

The "upper group" patient (≥20% extrasystoles) demonstrated significantly enlarged LV dimension, reduced LV ejection fraction, increased mitral regurgitation, and deteriorated New York Heart Association functional class as compared with the group of patients with <20% extrasystoles ("middle group" plus "lower group"). In contrast, parameters of LV function did not differ in the middle and low subgroups. Interestingly, of the three patients with unsuccessful RFA, only the patient from the "upper group" exhibited hemodynamic parameters that continued to deteriorate during follow-up, whereas no significant changes were noted in the other two patients from the "middle group."

The second important finding in the study of Takemoto et al. (23) relates to the dramatic improvement of all altered parameters of LV function after RFA only in the subgroup of patients with the highest level of ventricular ectopic activity at baseline (≥20% per 24 h, grossly ≥20,000 beats per day). In that group, the hemodynamic parameters after ablation became similar to those observed in the two other groups (<20% extrasystoles) before ablation. The results obtained in the largest cohort of patients with frequent and complex RVOT arrhythmias who have been evaluated before and after RFA confirm previous observations in a few cases that ablation of a ventricular focus could reverse LV dysfunction in some patients with cardiomyopathy.

Takemoto et al. (23) made interesting comments on the potential mechanism of LV dysfunction resulting from high-grade ventricular RVOT arrhythmias with special emphasis on the left bundle branch block configuration of the arrhythmia. In this regard, it is interesting to note that all previous reports of LV dysfunction associated with high-grade idiopathic ventricular arrhythmias have involved right ventricular arrhythmias (13–18). It is possible that LV dysfunction results from the cumulative effects of arrhythmia-related LV dyssynchronization (left bundle branch block pattern of LV depolarization) and mimics the degree of LV dysfunction related to the cumulative percentage of right ventricular pacing, as recently documented in the Model Selection Trial (MOST) (24). There also may be a superimposed element of tachycardia-induced cardiomyopathy linked to the cardiac short cycles truncated by extrasystoles.

How will the results of the study by Takemoto et al. (23) affect our treatment of complex idiopathic RVOT arrhythmias? For patients who present with LV dysfunction and frequent arrhythmias, the data should provide justification for recommending RFA of the ventricular focus. A successful ablation will probably result in complete or partial resolution of the cardiomyopathy. Such patients should have regular Holter recordings after successful RFA to detect asymptomatic arrhythmia recurrence. For patients with ventricular arrhythmias associated with normal LV function, the data would suggest adopting an aggressive approach in patients with very frequent ventricular extrasystoles (>20% per 24 h). For other patients, RFA cannot be justified on the basis of the present data. An answer to this question requires a randomized study comparing long-term echocardiographic data after either no therapy or RFA. Until such a study is available, the decision to ablate should be made individually after careful consideration of the advantages and disadvantages of the procedure as well as of the patient's choice. In view of the quite-low complications and high success rate of RFA in experienced centers, it will certainly be tempting to recommend RFA of a worrisome and potentially deleterious arrhythmia, especially in young women before childbearing or in any young patient who "wants to have a normal ECG and Holter, like everybody else!"

Takemoto et al. (23) have added a new dimension to the treatment of RVOT arrhythmias. Not all extrasystoles are equal in that some "benign" right ventricular extrasystoles may not be so benign after all but are amenable to RFA therapy. Thus, it seems that RFA of ventricular extrasystoles has finally "found its disease" in terms of the extrasystolic development of disturbed LV dysfunction.

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